DETAILED ACTION

The receipt is acknowledged of applicant's IDS filed 08/30/2006, and election filed 02/03/2010.

Claims 1-20 are pending.

Election/Restrictions

1. Applicant's election without traverse of invention I, species (b) of unsaturated fatty acid permeation enhancer, claims 1-7, 9, 10, 14, 17, 18, in the reply filed on 02/03/2010 is acknowledged.

2. Claims 8, 11-13, 15, 16, 19, and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention an species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 02/03/2010.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-7, 9, 10, 14, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jona et al. (US 5,891,461, IDS filed 08/30/2006) in view of Kanios et al. (US 2005/0169977, current PTO 892).

Applicant Claims

Applicant's claim 1 is directed to a transdermal drug delivery composition comprising:

(a) a pressure sensitive adhesive comprising a copolymer comprising copolymerized monomers, wherein said monomers comprise a first monomer selected from isooctyl acrylate, ethyl hexyl acrylate, n-butyl acrylate and combinations thereof, and a second monomer selected from acrylamide, vinyl acetate, hydroxy ethyl acrylate, acrylic acid, and combinations thereof;

(b) at least one excipient selected from amine oxides, unsaturated fatty acids, isopropyl myristate, lauroglycol, a-terpineol, polyethylene glycol, sorbitan esters, lactic acid, dimethylsulfoxide, and combinations thereof; and

(c) olanzapine or a pharmaceutically acceptable salt thereof.

Determination of the Scope and Content of the Prior Art

(MPEP §2141.01)

Jona teaches transdermal device for administration of olanzapine to treat schizophrenia, psychosis, and acute mania for a time period and rate of administration effective to alleviate symptoms of the disease (abstract). Jona teaches transdermal device comprising backing layer and adhesive matrix containing olanzapine and skin permeation enhancer (col.3, lines 37-50; col.4, lines 6-19). Olanzpine can be administered in its free base form (col.6, lines 16-17). Enhancers include fatty acids such as oleic acid (col.6, lines 31-32, 66; tables 3, 4, 6, 7). Adhesive matrix includes polyacrylates (col.8, line 14). The reference does not disclose any undissolved olanzapine in the formulation, i.e. all the drug is dissolved in the matrix layer.

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Although Jona teaches polyacrylate adhesive matrix, however, does not explicitly teach the copolymer as instantly claimed by claim 1. Although Jona teaches administration of the olanzapine transdermal device for a time period and rate of

administration effective to alleviate symptoms of the disease, however, does snot explicitly teach the period of time as instantly claimed by claim 18.

Kanios teaches a transdermal delivery system to optimize drug loading while providing desirable adhesion to skin or mucosa as well as providing modulation of the drug delivery, permeation rate and profile. The transdermal drug delivery system comprises drug containing layer and backing layer. The drug containing layer comprises acrylic-based polymers comprising one or more monomers of acrylic acids and other copolymerizable monomers. Acrylate monomers include isooctyl acrylate, butyl acrylate, and ethylhexyl acrylate. Monomers copolymerizable with the above acrylates include acrylic acid, hydroxyethyl acrylate and vinyl acetate. The delivery rate, onset of delivery and delivery profile of a drug are selectively modulated by manipulating the moiety or functionality of the acrylic-based polymer, and manipulating the monomeric composition and/or ratios of the acrylic- based polymer. The reference teaches that drugs can be present in the composition in different forms, depending on which yields the optimum delivery characteristics. Thus, the drug can be in its free base form or in the form of salts, esters, or any other pharmacologically acceptable derivatives. Drugs include benzodiazepines. (See abstract; paragraphs 0016, 0017, 0020, 0037, 0050-0058, 0067, 0085, 0103, 105).

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP §2142-2143)

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide transdermal device for administration of olanzapine to treat schizophrenia, psychosis, and acute mania comprising backing layer and polyacrylate adhesive matrix containing olanzapine and oleic acid as skin permeation enhancer as taught by Jona, and replace the polyacrylate adhesive matrix with an acrylic-based polymers taught by Kanios comprising first monomer selected from isooctyl acrylate, butyl acrylate, ethylhexyl acrylate and second monomers copolymerizable with the first monomer selected from acrylic acid, hydroxyethyl acrylate and vinyl acetate. One would have been motivated to do so because Kanios teaches that such acrylic-based polymers provide the desirable adhesion to skin as well as selective modulation of the drug delivery, permeation rate and profile by manipulating the moiety or functionality of the acrylic-based polymer, and manipulating the monomeric composition and/or ratios of the acrylic- based polymer. One would reasonably expect formulating transdermal device for administration of olanzapine comprising backing layer and adhesive matrix containing olanzapine, oleic acid, and acrylic based polymer comprising first monomer selected from isooctyl acrylate, butyl acrylate, ethylhexyl acrylate and second monomers copolymerizable with the first monomer selected from acrylic acid, hydroxyethyl acrylate and vinyl acetate, wherein the acrylic-based adhesive matrix provides the desirable adhesion to skin as well as selective modulation of the olanzapine delivery, permeation rate and profile to treat schizophrenia, psychosis, and acute mania successfully and effectively.

Regarding the period of time of application of the device to the patient as claimed by claim 18, Jona teaches application of the device for a time period and rate of administration effective to alleviate symptoms of a disease including schizophrenia, psychosis, and acute mania. Kanios further teaches that the delivery rate, onset of delivery and delivery profile of a drug can be selectively modulated by manipulating the moiety or functionality of the acrylic-based polymer and/or adhesive coating, and manipulating the monomeric composition and/or ratios of the acrylic- based polymer. Therefore, the art recognized variation and manipulation of time and rate of delivery of a drug based on the specific intended use.

In any event, those of ordinary skill in the art would have been readily optimized effective dosages, period of treatment and concurrent administration regimens as determined by good medical practice and the clinical condition of the individual patient. Determination of the period of application of a transdermal device involving treatment of the schizophrenia or bipolar mania would have been routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the disclosure of Jona and Kanios. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the

instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

IG

/Isis A Ghali/
Primary Examiner, Art Unit 1611